

Figure 1 Commonly used glycosylating agents

09933277.081701

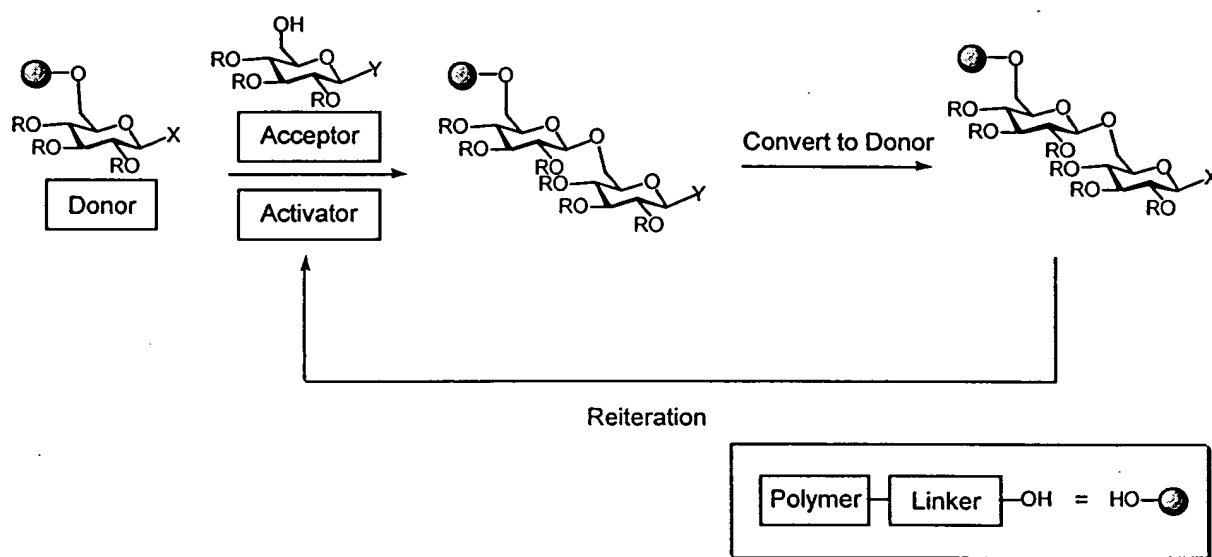


Figure 2 Donor bound solid-phase carbohydrate synthesis

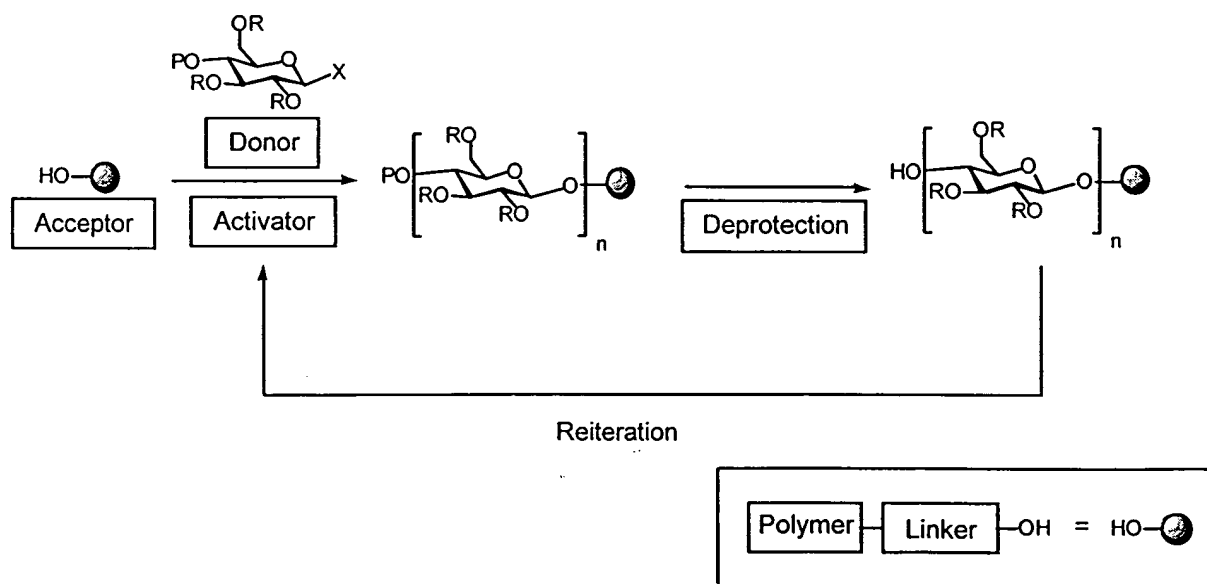
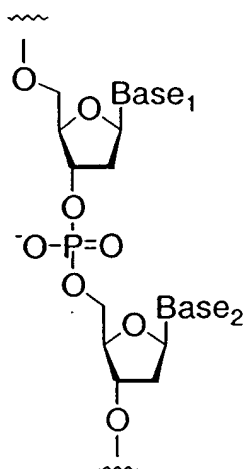


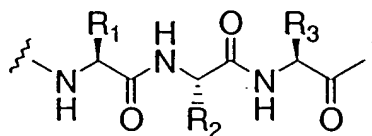
Figure 3 Acceptor bound solid-phase carbohydrate synthesis

Figure 4

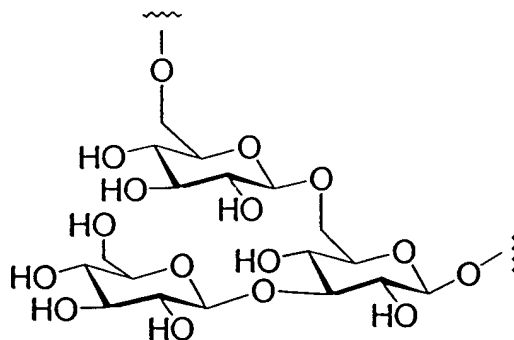
a) oligonucleotides



b) oligopeptides



c) oligosaccharides



Automated Oligosaccharide Synthesizer

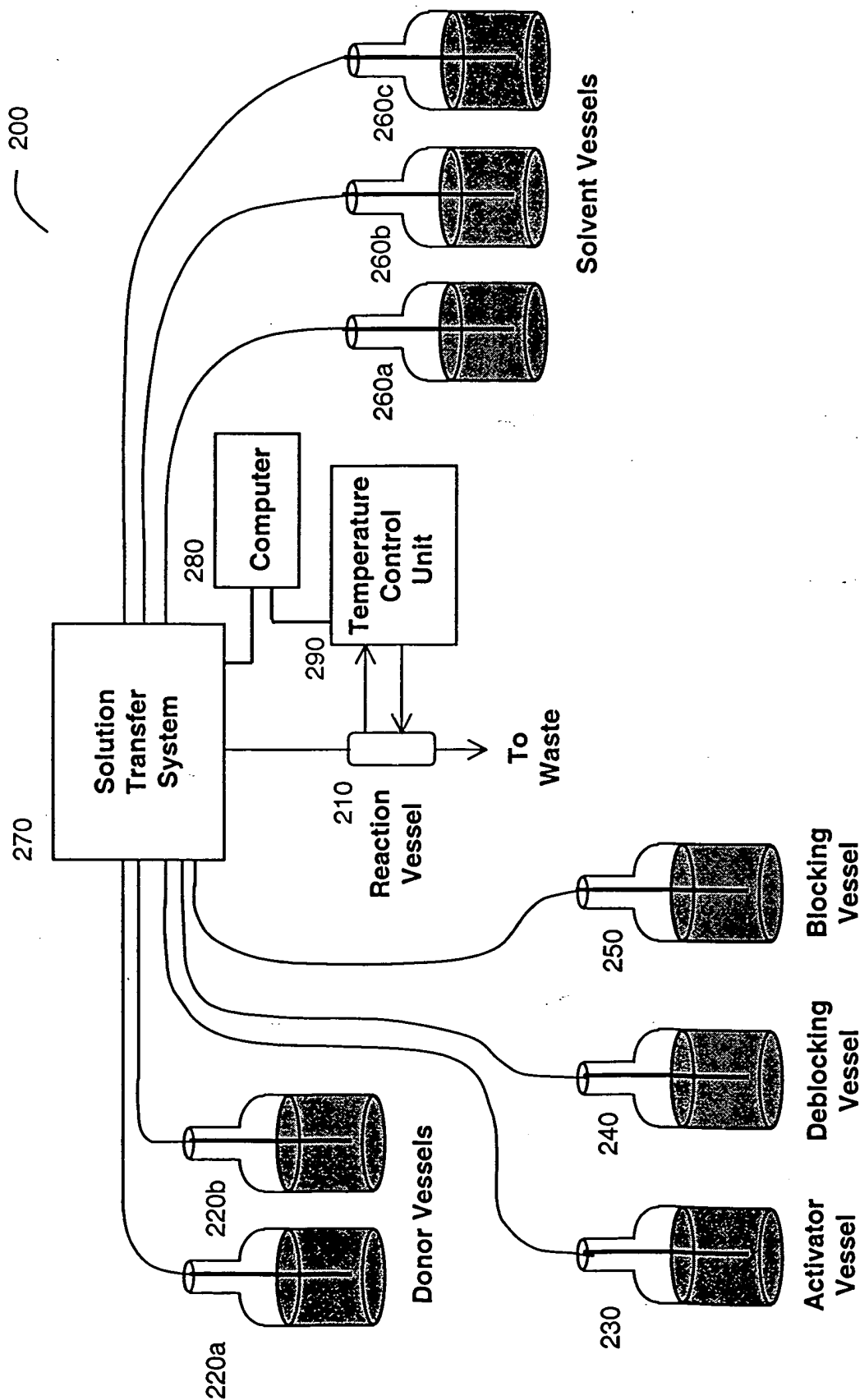


Figure 5

Automated Oligosaccharide Synthesizer

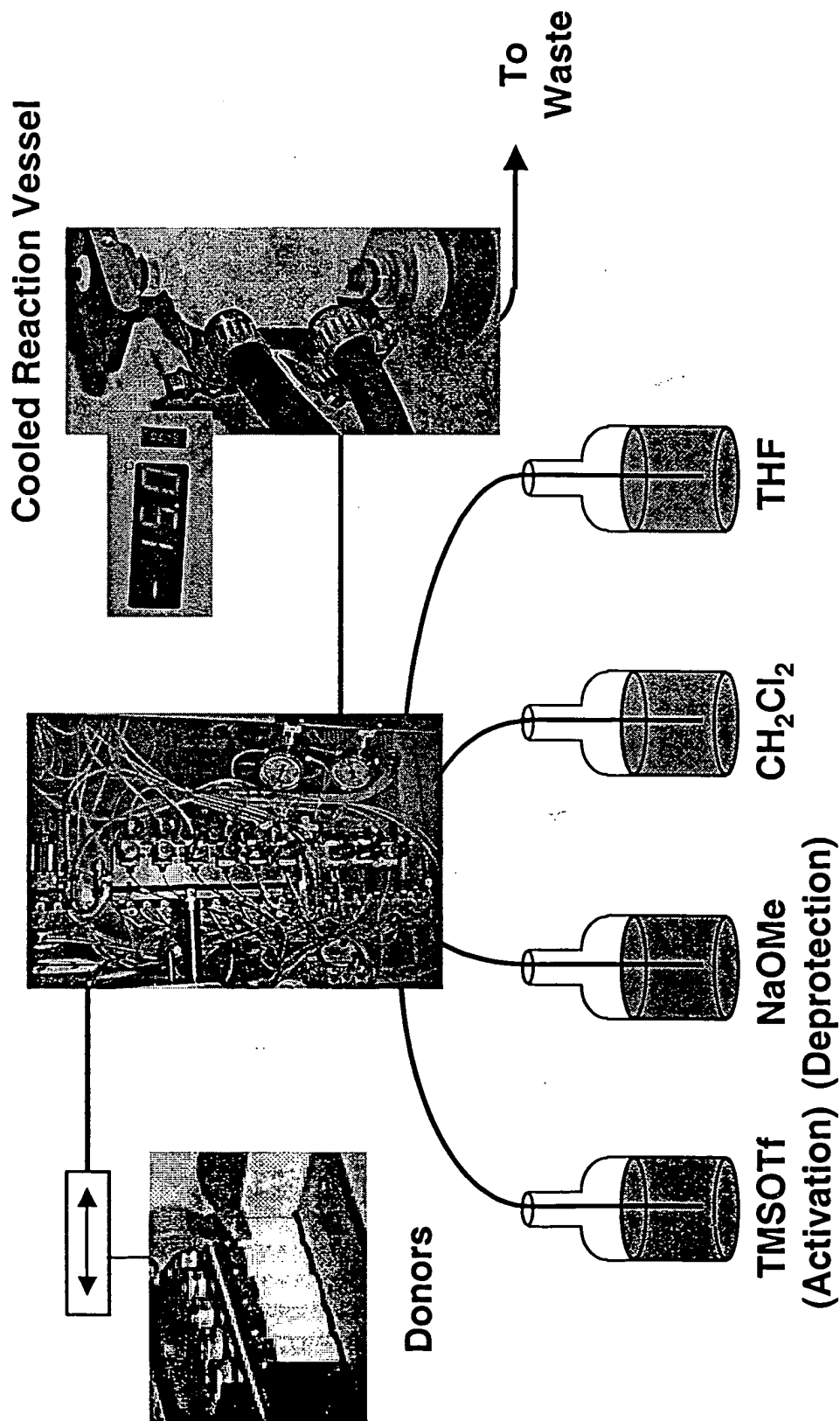


Figure 6

Double-Walled Cooled Reaction Vessel

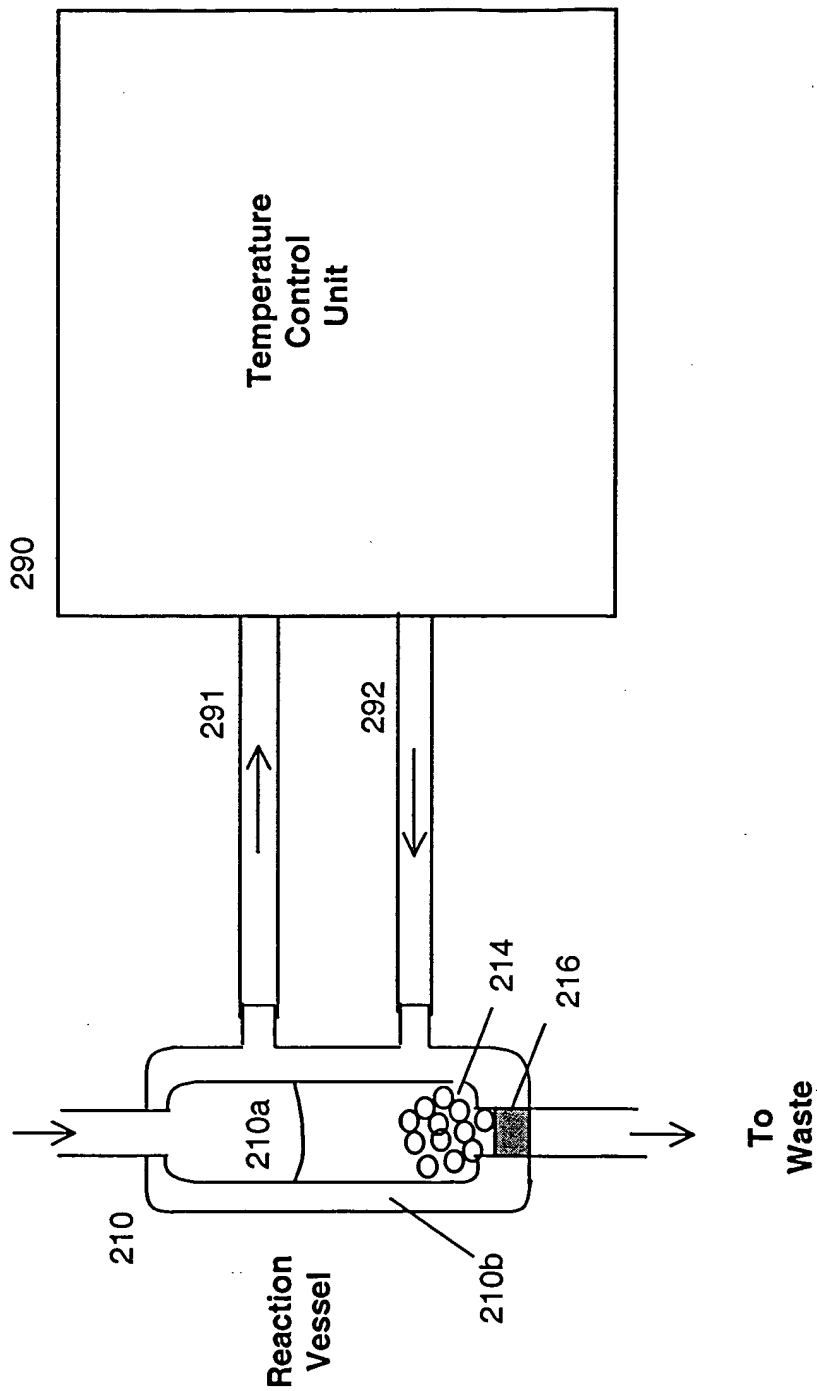
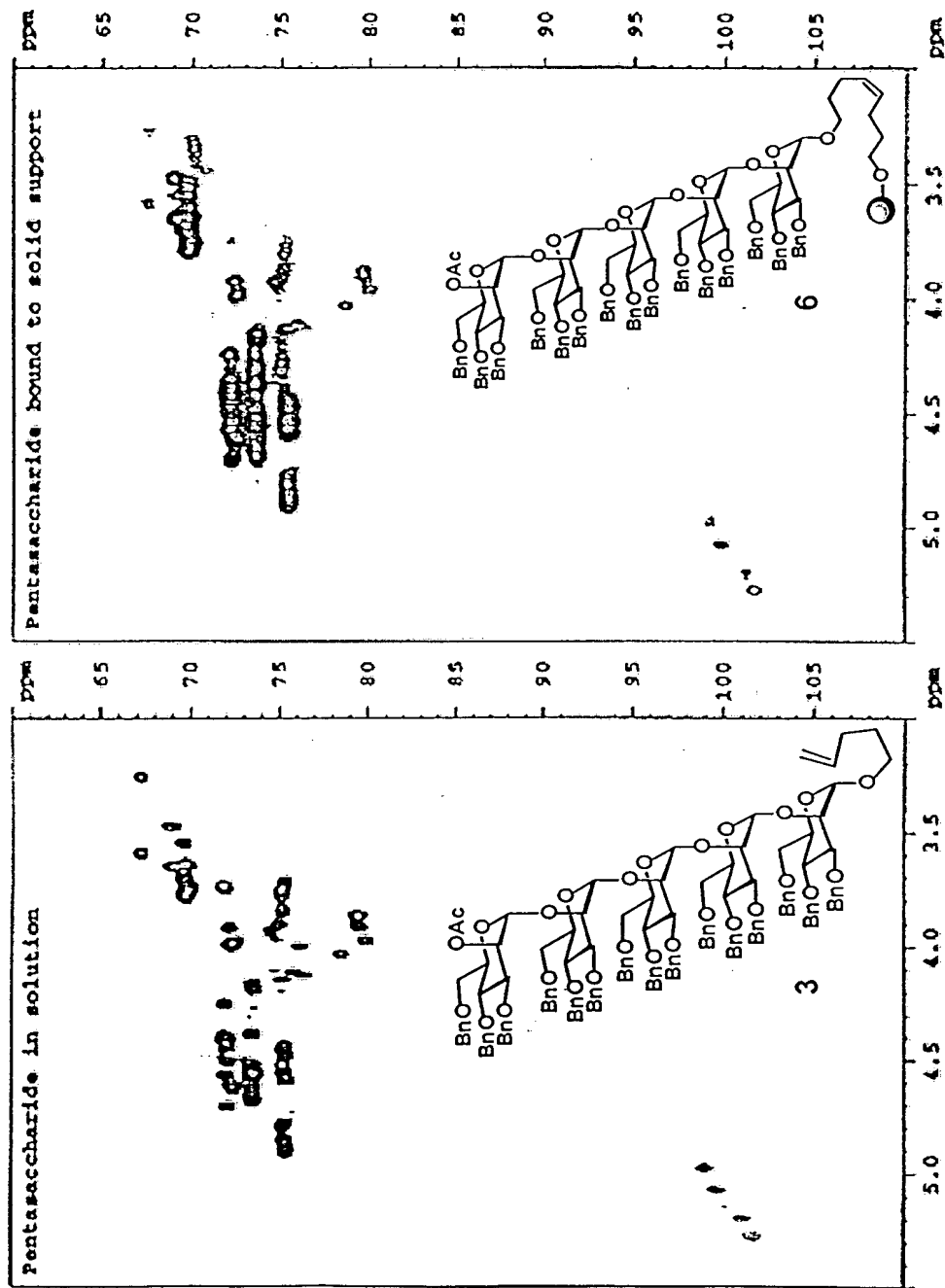
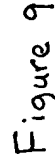


Figure 7

Figure 8

2D-NMR comparison of resin bound and solution phase pentamer





Garegg et al. *Angew. Chem. Int. Ed.* 1983, 22, 793;

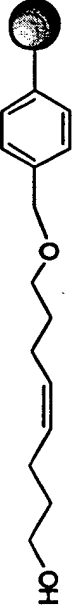
on soluble support: van Boom et al. *Recl. Trav. Chim. Pays-Bas* 1993, 112, 464;

on polymer support using trisaccharide blocks: Nicolaou et al. *Angew. Chem. Int. Ed.* 1998, 37, 1559.

Figure 10

Automated Oligosaccharide Synthesis

Chemical Issues:

- Choice of Resin (Merrifield's, Argopore, Tentagel)
- Linker: 
- Glycosylation Protocol
- Deprotection Protocol
- Capping Cycle
- Cleavage Method
- Purification Technique

Practical Issues:

- Scale (μmol - mmol)
- Cycle Development/Time
- Temperature Control Device

Automated Oligosaccharide Synthesis with Glycosyl Phosphates: Coupling Cycle

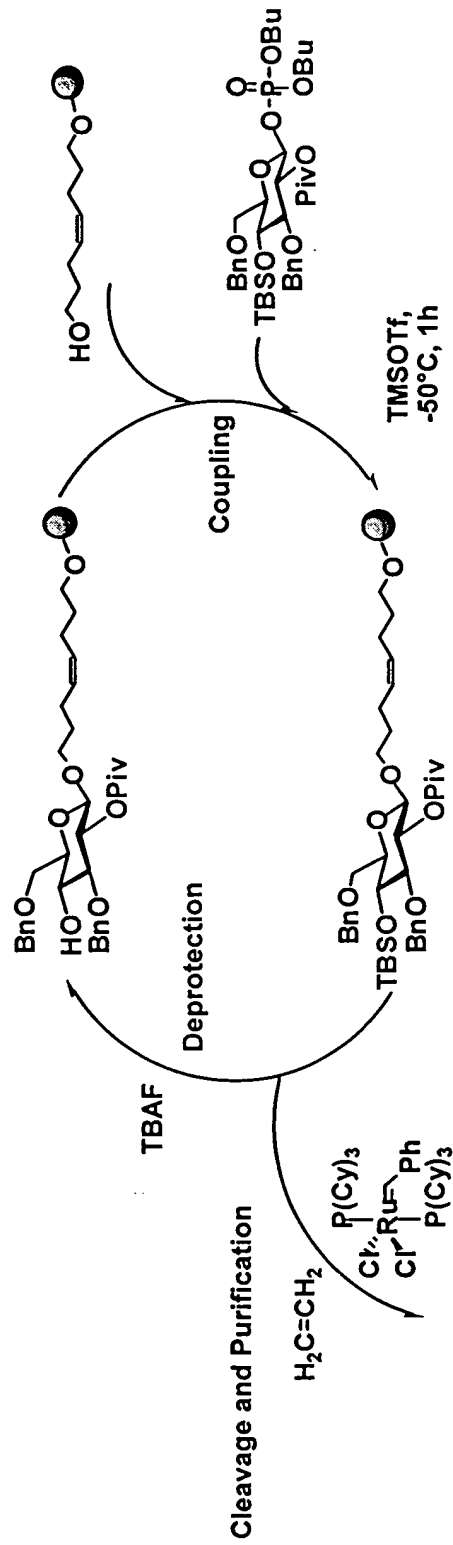
	Reagent/Solvent	Equivalents	Temperature	Time
Coupling	Donor TMSOTf	5 5	-15 °C	15 min
Washing	CH ₂ Cl ₂ THF			5 min
Coupling	Donor TMSOTf	5 5	-15 °C	15 min
Washing	CH ₂ Cl ₂ THF			5 min
Deprotection	N ₂ H ₄ -HOAc		15 °C	30 min
Washing	Pyr./AcOH			5 min
Deprotection	N ₂ H ₄ -HOAc		15 °C	30 min
Washing	Pyr./AcOH			5 min

Figure 11

Cycle Time per residue 110 min

Figure 12

Solid Support Oligosaccharide Synthesis: Glycosyl Phosphate Donors

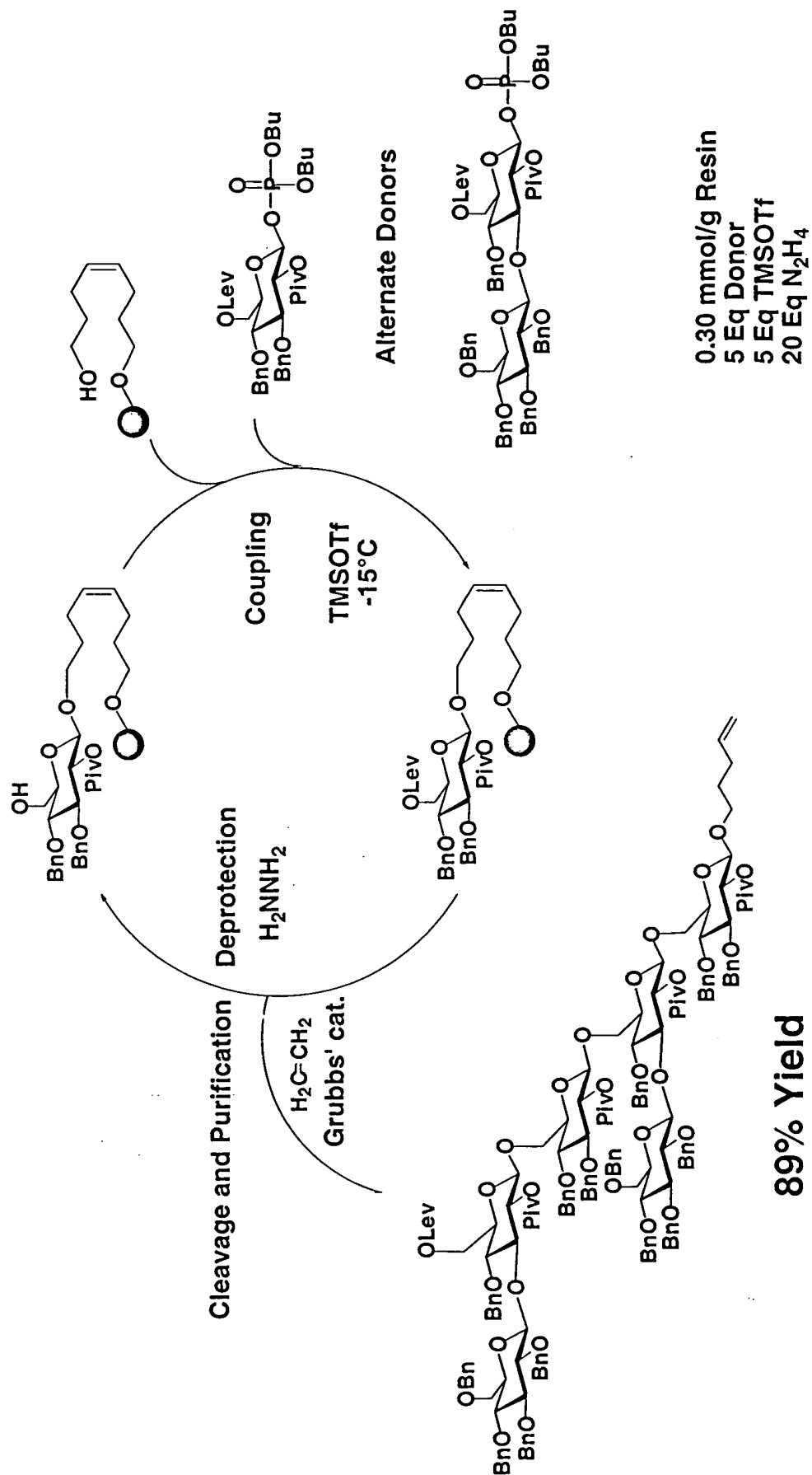


53% overall yield

- Advantages:**
- excess reagents drive reactions to completion
 - purification only at the end of the synthesis

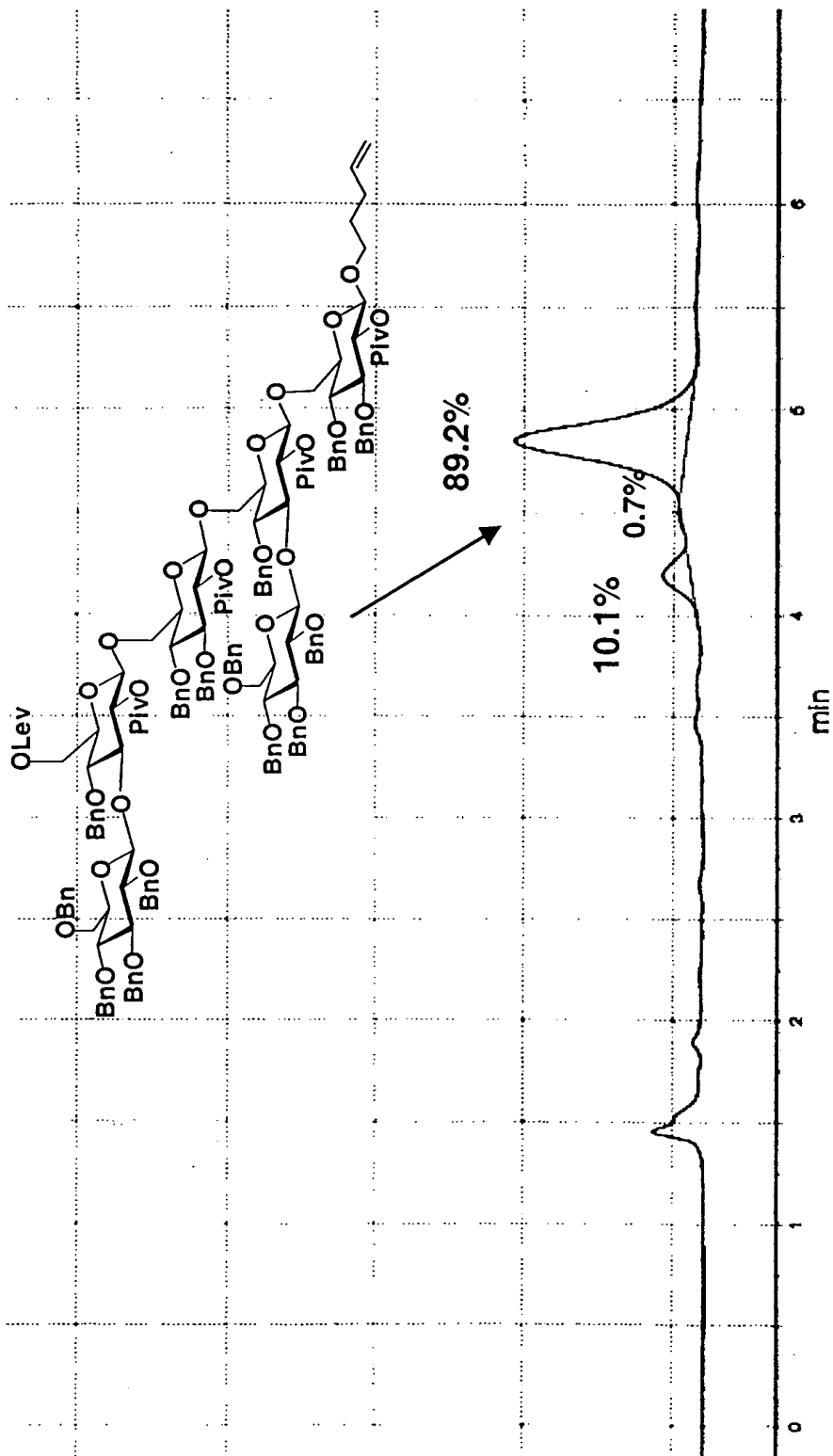
Figure 13

Automated Hexasaccharide Synthesis Using Glycosyl Phosphates



Crude HPLC Profile of the Hexamer Synthesis

Figure 14



Automated Oligomannoside Synthesis:

Coupling Cycle

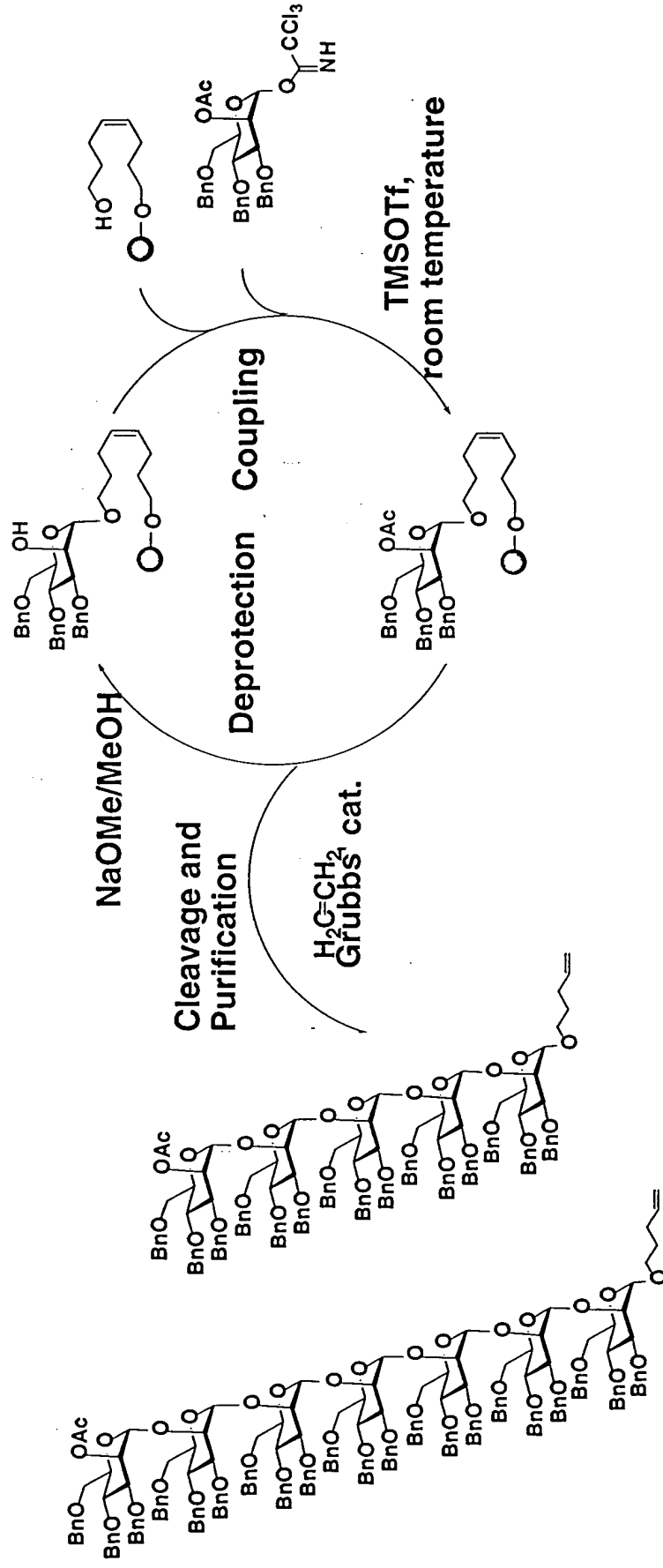
Figure 15

	Reagent/Solvent	Equivalents	Time
Coupling	Donor TMSOTf	10 0.5	30 min
Washing	CH ₂ Cl ₂ THF		5 min
Coupling	Donor TMSOTf	10 0.5	30 min
Washing	CH ₂ Cl ₂ THF		5 min
Deprotection	NaOMe		30 min
Washing	CH ₂ Cl ₂ THF		5 min
Deprotection	NaOMe		30 min
Washing	CH ₂ Cl ₂ THF		5 min
Cycle Time per residue			140 min

25 μmol Scale

Solid-Phase Oligosaccharide Synthesis: Coupling Cycle Development

Figure 16



42% yield 74% yield

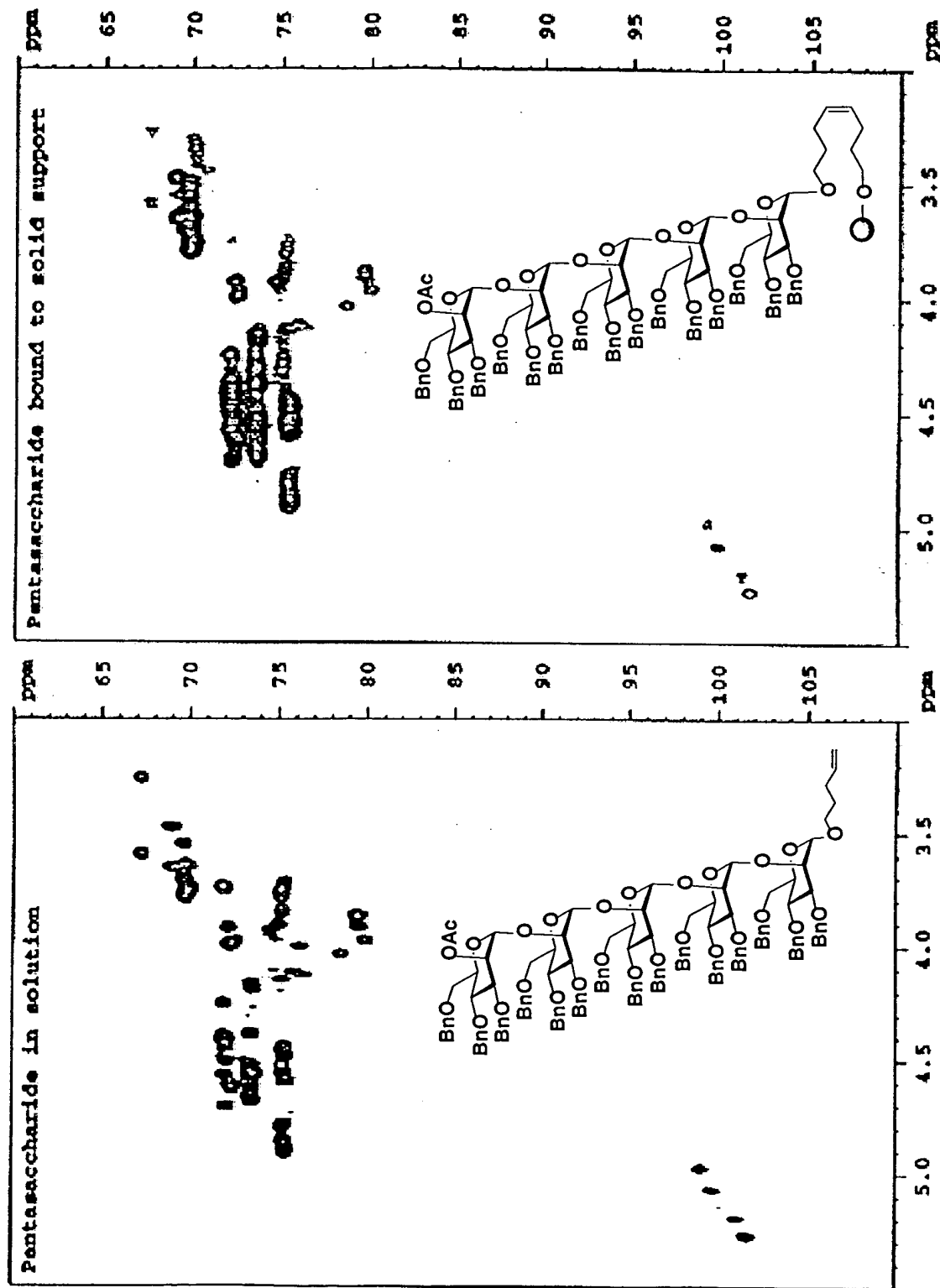
(manual synthesis: 9%)

stepwise yield: 94% stepwise yield: 94%

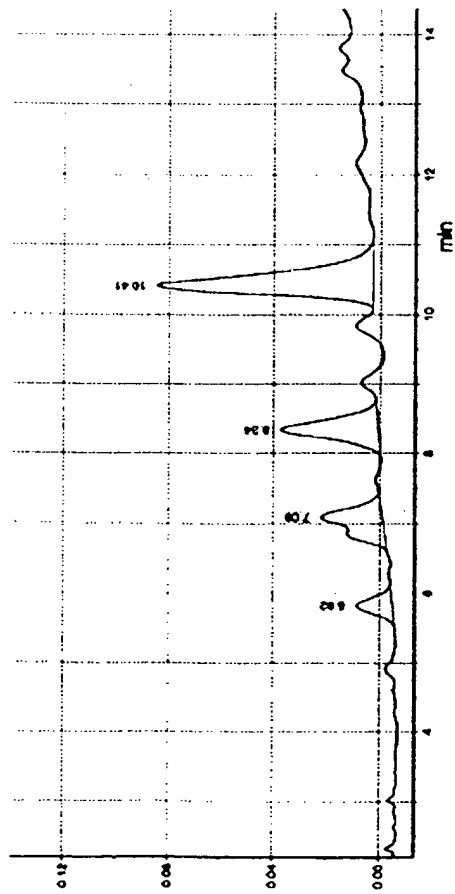
FOI b7D 222550

Figure 17

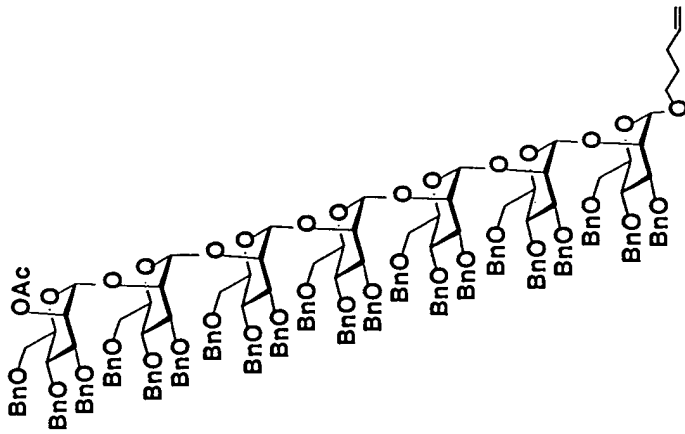
HR-MAS HMQC-Analysis of Pentamannosides



HPLC Purification of the Heptamannoside



Crude



42% Yield

Pure

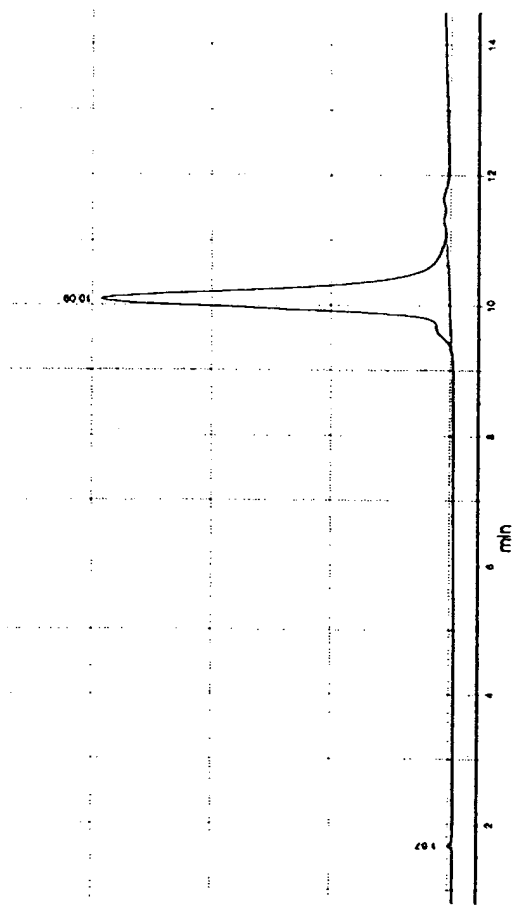
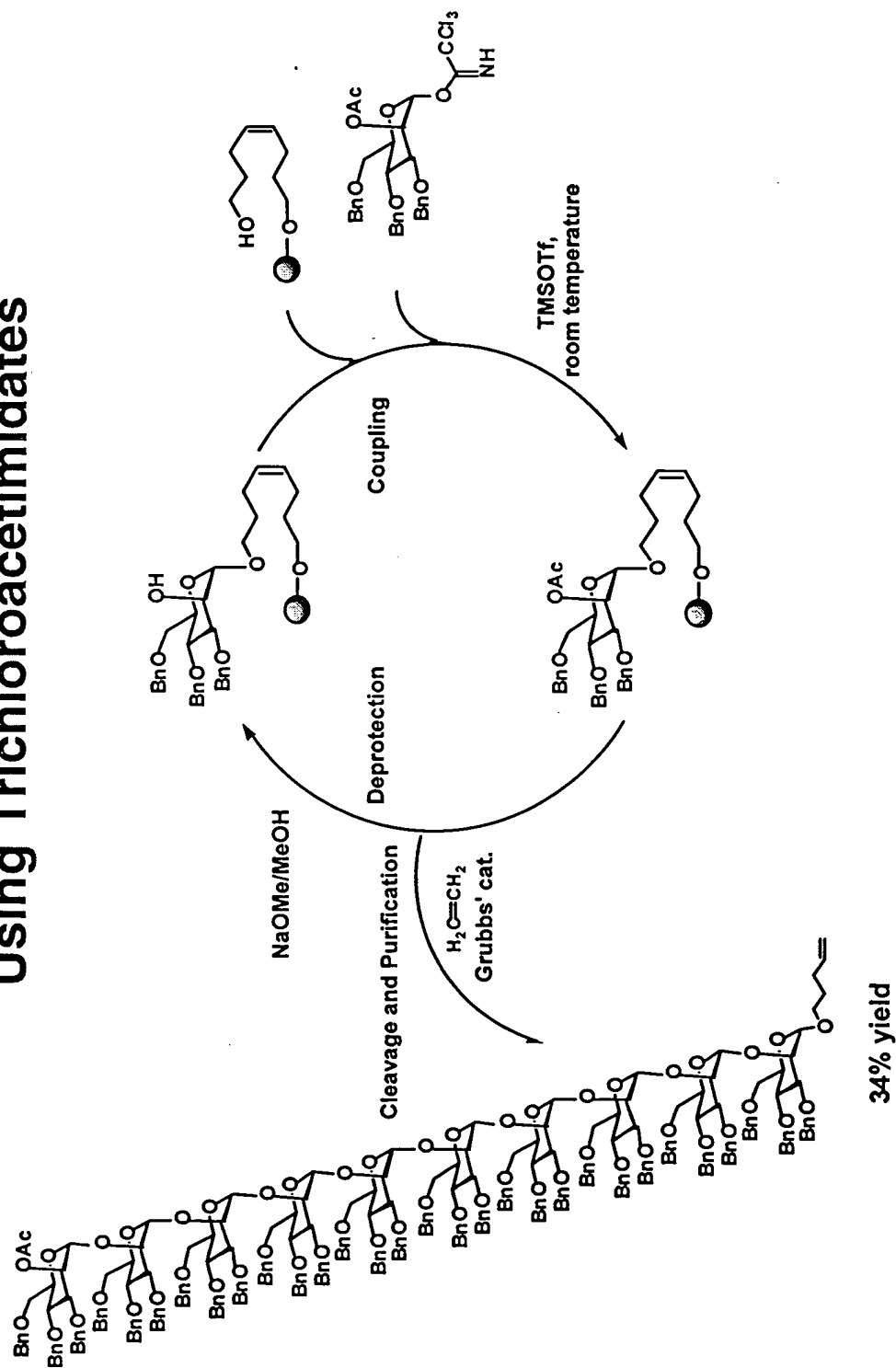


Figure 19

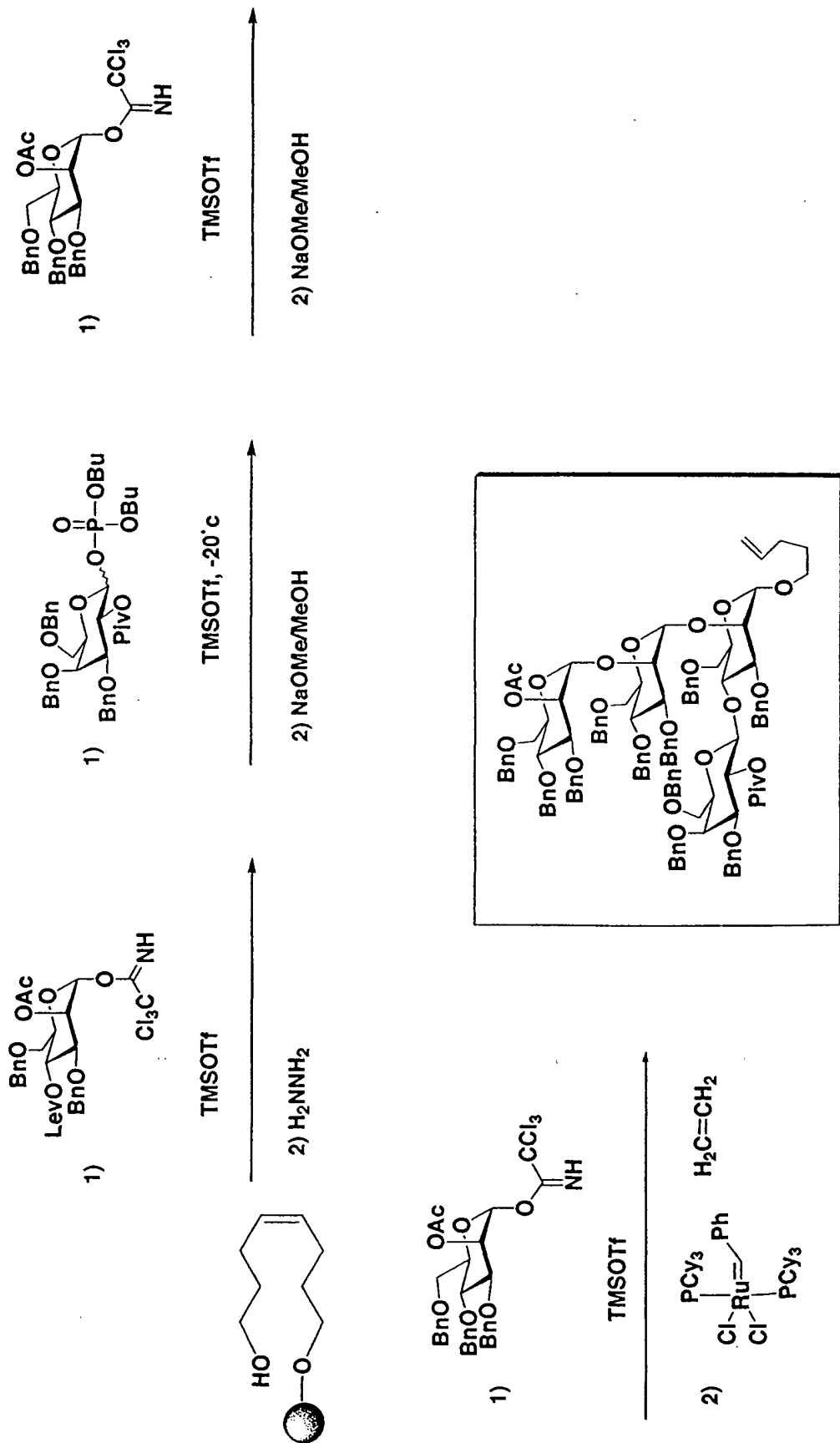
Automated Synthesis of a Decamannoside Using Trichloroacetimidates



stepwise yield: 94.9%

Figure 20

Automated Synthesis of Leishmania Cap Tetrasaccharide



66% yield

Automated Synthesis of polyglucosamines

